

1 **Transanal Total Mesorectal Excision for Primary Rectovaginal Carcinosarcoma: A Case**

2 **Report and Literature Review**

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24 **Short running title:** TaTME for rectovaginal carcinosarcoma

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35 Abstract

36 We report a case of rectovaginal septum carcinosarcoma successfully treated with
37 surgical excision via transanal total mesorectal excision following platinum-based
38 neoadjuvant chemotherapy. A 48-year-old woman presented with a 3-week defecation pain
39 preceding the visit. Pelvic imaging showed an 8-cm-sized lesion in the lower rectovaginal
40 septum. Transvaginal biopsy and immunohistochemical analysis were performed. After three
41 courses of carboplatin-paclitaxel-bevacizumab therapy, the mass reduced by half.
42 Subsequently, laparoscopic excision with transanal total mesorectal excision, and radical
43 hysterectomy were performed. The anus was preserved, and dysuria improved within a
44 month. The final histopathological diagnosis was carcinosarcoma of the rectovaginal septum
45 from an uncertain origin, presumably endometriotic or mesonephric. Twelve months
46 following surgery, solitary liver metastasis was confirmed; however, there was no evidence of
47 local recurrence.

48 Total mesorectal excision following platinum-based neoadjuvant chemotherapy may be an
49 ideal treatment for gynecological malignancies in the rectovaginal septum, especially for
50 large tumors localized deep into the pelvis.

51 **Keywords:** carcinosarcoma, neoadjuvant chemotherapy, platinum-based neoadjuvant

52 chemotherapy, rectovaginal malignancy, transanal total mesorectal.

53

54 **Introduction**

55 Primary malignancy of the rectovaginal septum (PMRS) is a remarkably rare
56 presentation, with the exception of gastrointestinal stromal tumors (GIST). A few cases of
57 PMRS have been described in the literature, and adjuvant chemotherapy or radiation therapy
58 following radical surgery, aimed at R0 resection has been performed.¹⁻⁸ However, it is
59 difficult to achieve complete resection with sufficient surgical margins while preserving
60 urinary or anal function in these procedures, especially when the tumor is large and located in
61 the low rectovaginal septum.

62 Recently, transanal total mesorectal excision (TaTME) has been proposed as a technique to
63 achieve both sufficient tumor resection and functional preservation in the surgical treatment
64 of low and large rectal cancer.^{9,10} TaTME is a technique in which an endoscope and forceps
65 are inserted through the anus, in addition to the typical abdominal approach. TaTME's
66 several benefits over laparoscopic surgery include the exposure of the distal rectum and direct
67 determination of distal resection margin. In addition, operation time can be significantly
68 reduced if two teams perform the operation simultaneously, one from the abdominal cavity

69 and the other from the anus.

70 Neoadjuvant chemotherapy (NAC) prior to definitive surgery is an alternative treatment

71 option for patients with advanced epithelial ovarian cancer. Expected benefits include

72 reduced perioperative morbidity and mortality and increased likelihood of a complete

73 resection of disease at the time of cytoreductive surgery.^{11,12} However, the effects of NAC

74 on PMRS remain unclear.

75 Here, we report a patient with carcinosarcoma of the rectovaginal septum who was

76 successfully treated with surgical excision using TaTME following platinum-based NAC.

77

78 **Case Report**

79 The patient provided informed consent for publication of this case. A 48-year-old

80 woman (gravida 2, para 2) with a history of bilateral salpingo-oophorectomy due to pelvic

81 endometriosis presented with pain on defecation to our hospital. Upon internal examination, a

82 large mass was discovered on the back side of the posterior vaginal wall. Vaginal ultrasound

83 and magnetic resonance tomography (MRI) revealed an 80 × 71 × 70 mm pelvic mass

84 suggestive of a malignant tumor of the rectovaginal septum, with no obvious distant

85 metastasis found on computed tomography (Fig. 1 A, B). The mass was involved in a section

86 of the levator ani muscle on the right side (Fig. 1 C). Adenocarcinoma was detected via
87 transvaginal needle biopsy of the tumor. Immunohistochemical assessments of the tumor
88 cells for cytokeratin (CK) 7 and paired-box gene (PAX8) were positive, and those for CK 20,
89 estrogen receptor, progesterone receptor, Wilms tumor gene 1, and hepatocyte nuclear factor-
90 1 beta were negative. Serum levels of Ca125 and Ca19-9 were normal, while
91 carcinoembryonic antigen was mildly elevated (13.0 ng / mL).

92 Three courses of carboplatin-paclitaxel-bevacizumab (CP+Bev) therapy were administered
93 as NAC. An MRI scan following NAC revealed a clear contraction of the tumor ($80 \times 71 \times$
94 70 mm to $42 \times 32 \times 41$ mm) (Fig. 1 D, E). After comprehensive counselling, the patient was
95 scheduled for surgical removal using TaTME.

96 TaTME was performed by two teams: an anal approach and traditional laparoscopic teams.
97 On traditional laparoscopic inspection, no disseminated lesions were found. First, GelPOINT
98 path transanal access platform (Applied Medical, Rancho Santa Margarita, CA, USA) was
99 inserted into the pneumorectum system in the lithotomy position under general anesthesia.

100 We used the GelPOINT Path Transanal Access Platform and AirSeal (ConMed, Utica, NY,
101 USA) as insufflation systems to obtain a stable pneumorectum with smoke evacuation. The
102 lumen of the rectum was closed at the upper edge of the anal canal with a purse-string suture

103 to prevent mucus leakage (Fig. 2A). The endopelvic fascia was identified after
104 intersphincteric resection of the muscle, and a section of the levator ani muscle on the right
105 side was excised. After the hiatal ligament was dissected, the total mesorectal excision (TME)
106 plane was revealed using a transanal approach. The traditional laparoscopic team inserted
107 five ports in parallel, and the round, infundibulopelvic, and transverse cervical ligaments
108 were separated. TME was also performed on the abdominal side. First, the trans-anal and
109 trans-abdominal layers conformed to each other on the back side, and later coincided in all
110 directions (Fig. 2B). The pelvic splanchnic nerves visceral branch of the right S3 and S4 were
111 involved in the tumor, and were resected together; however, the lower abdominal nerve, other
112 roots of the S3 and S4, and obturator nerve was preserved. The rectovaginal tumor was
113 completely excised along with the uterus, vaginal wall, and rectum via en bloc resection (Fig.
114 2C). Finally, anal canal-sigmoid anastomosis was performed and a covering ileostomy was
115 constructed (See supplement movie file). The operation took a total of 521 min, and the blood
116 loss was 500 mL. There were no intra or post-operative complications, and the patient was
117 discharged from the hospital 12 days after surgery. Initially, the patient required self-control
118 due to post-operative dysuria; however, this improved within 1 month and self-control was
119 terminated. The histopathological diagnosis was carcinosarcoma arising from the

120 rectovaginal septum of uncertain origin, presumed to be of endometriosis or mesonephric
121 rests. The surgical margins were negative, and the patient was treated with adjuvant CP + Bev
122 therapy for three cycles and continued to receive Bev maintenance therapy following the final
123 course of CP + Bev therapy. Twelve months following surgery, solitary liver metastasis was
124 confirmed; however, there was no evidence of local recurrence. Partial liver resection and
125 closure of the ileostomy are required in the future.

126

127 **Discussion**

128 To the best of our knowledge, this is the first report of PMRS successfully treated
129 with surgical excision by TaTME following platinum-based NAC. TaTME was useful in the
130 surgical resection of malignant tumors of the rectovaginal septum in this case. The
131 effectiveness of NAC for rectovaginal malignancies has not yet been established; however,
132 this case suggests that NAC should be considered to achieve both functional preservation and
133 effective resection.

134 Several cases of PMRS have been described in the literature (Table 1), excluding GIST.^{1-8,}

135 ¹³⁻¹⁷ As presented in Table 1, 13 of the 15 patients studied had adenocarcinomas. The trends

136 of CK7(+), PAX8(+), and CK20(-) indicate that the tumors were of gynecological origin, for

137 example, from endometriosis or the mesonephric duct; however, not all
138 immunohistochemical results were available from these studies. Endometriosis is believed to
139 be the major developmental basis for such cancers. Seven of the 15 cases histologically
140 coexisted with endometriosis. The remaining eight were described as unrelated to
141 endometriosis; however, existing endometrial tissues and endometriomas may have been
142 destroyed by the invasion of cancer. In addition, it has been proposed that such lesions could
143 originate from mesonephric rests¹⁸. In the present case, the histological type of the
144 carcinosarcoma, and results of immunohistopathology were not contrary to endometriosis or
145 mesonephric rest-related malignancies¹⁹.

146 Primary debulking surgery, with or without adjuvant chemotherapy or irradiation, has been
147 commonly performed for gynecological PMRS (Table 1). In previous studies, patients were
148 treated with radical or preoperative (chemo) radiation therapy. Three of the patients who
149 underwent primary debulking surgery were treated laparoscopically, with the tumors
150 successfully resected. Furthermore, all three cases involved tumors of the upper rectovaginal
151 septum. In our case, as the tumor was located at the lower part of the rectovaginal septum,
152 making it difficult to secure sufficient margins and preserve the function of the pelvic organs
153 with conventional surgical methods. Therefore, TaTME was selected for radical debulking

154 surgery. Moreover, as TaTME ensures an appropriate circumferential resection margin with a
155 good field of view close to the anus, a reliable distal margin and autonomic nerve
156 preservation can be achieved (mainly the pelvic splanchnic nerve S4). In our case, R0
157 resection with adequate margins was histopathologically achieved. In addition, the function
158 of the anal sphincter was preserved, and urinary dysfunction was limited to temporary and
159 clean intermittent self-catheterization, which became unnecessary approximately 1 month
160 after surgery.

161 Platinum-based neoadjuvant chemotherapy, commonly administered for ovarian cancer,
162 should also be considered for gynecological PMRS, especially when the tumor is large. The
163 characteristics of PMRS arising from endometriosis or mesonephric rests are believed to be
164 similar to those of endometriosis-associated ovarian cancers. Therefore, gynecological PMRS
165 may be treated in the same manner as ovarian cancer. Furthermore, as preoperative reduction
166 in tumor size is particularly important for rectovaginal malignancies from the anatomical
167 viewpoint, NAC should be considered. However, in the case of clear cell carcinoma, which is
168 resistant to chemotherapy, NAC should be administered with caution. Therefore, pre-
169 treatment histological examination is mandatory.

170 In conclusion, TaTME appears to be the ideal treatment for malignant tumors in the

171 rectovaginal septum, especially for large tumors localized in the deep pelvis. In addition,
172 platinum-based NAC should be considered because it may improve the performance of
173 optimal radical surgery while retaining urinary and defecatory functions. This combined
174 approach could achieve optimal oncological outcomes and functional preservation in cases of
175 rectovaginal gynecological malignancies.

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180 **Disclosure**

181 There are no conflicts of interest to declare.

182

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- 238

239 **Figure Legends**

240 **Figure 1**

241 T2-weighted pelvic magnetic resonance imaging. (A, B) Sagittal and axial sections show a
242 large mass in the rectovaginal space. (C) At the lower end, the mass extended to the right
243 levator ani muscle. (D, E) Similar to sections A and B. Following NAC, there was a
244 significant decrease in the size of the mass (m: mass, u: uterus, v: vagina, r: rectum, red arrow
245 indicates the levator ani muscle).

246

247 **Figure 2**

248 (A), (B) Laparoscopic findings during TaTME. (A) The lumen of the rectum was closed at
249 the upper edge of the anal canal with a purse-string suture to prevent mucus leakage. (B) The
250 trans-anal and trans-abdominal layers conformed to one another at the back side (r; rectum, s;
251 sacrum).

252 (C) Operatively extracted specimen. The tumor was removed en block with the rectum,
253 uterus, and vagina (t; tumor, u; uterus, v; vagina, r; rectum)

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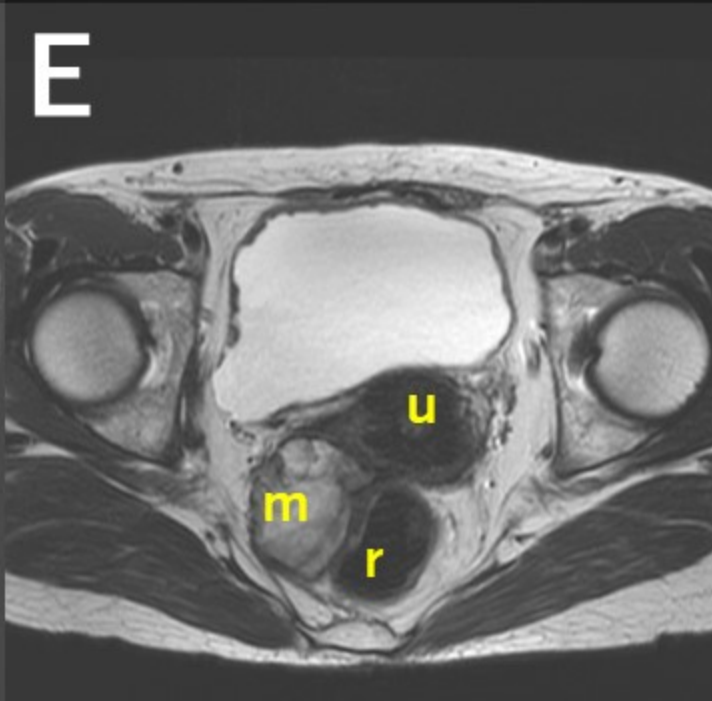
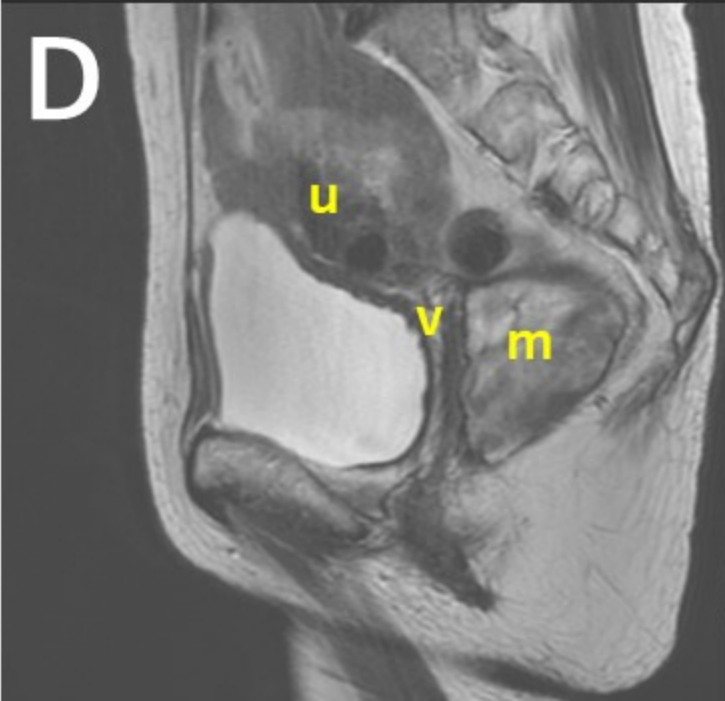
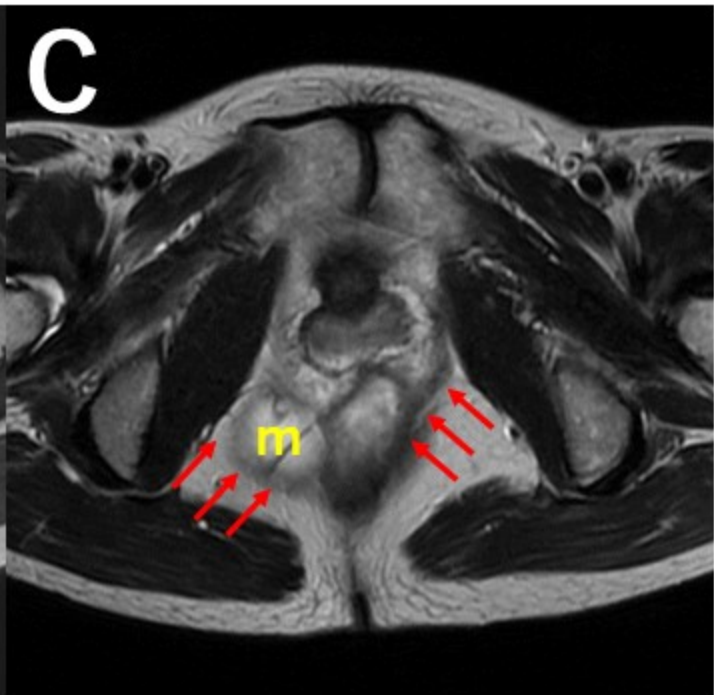
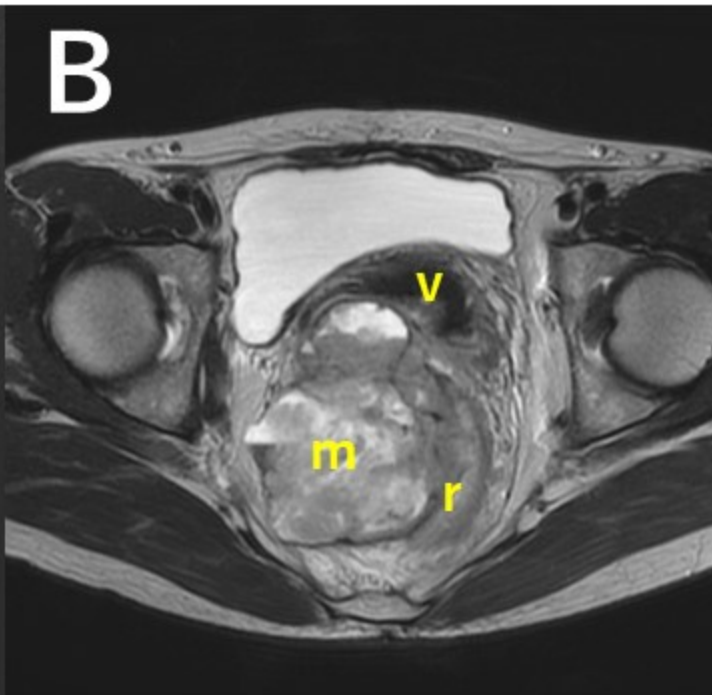
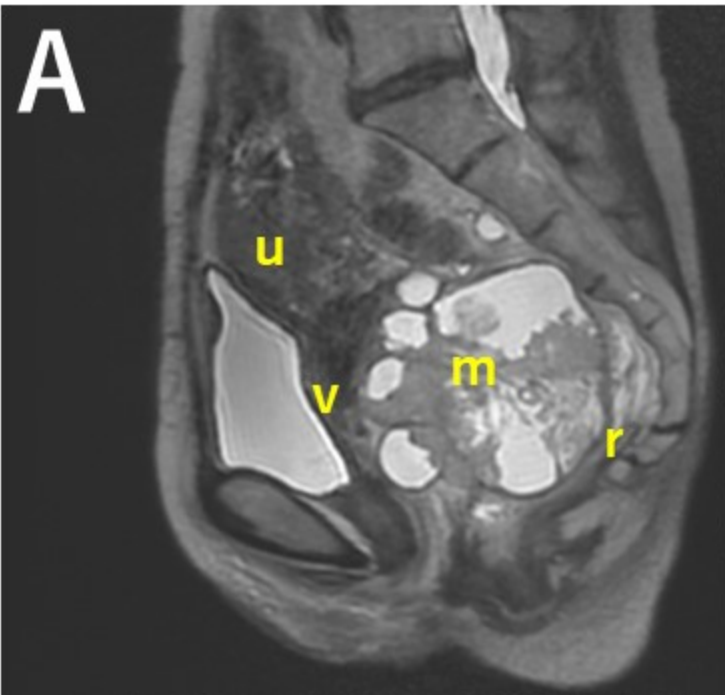
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256 **Supporting Information: Surgical video of TaTME**

257 TaTME was performed by two teams: an anal approach and traditional laparoscopic teams.

258 The rectovaginal tumor was completely excised along with the uterus, vaginal wall, and

259 rectum via en bloc resection. Anal sphincter and urinary function was preserved.



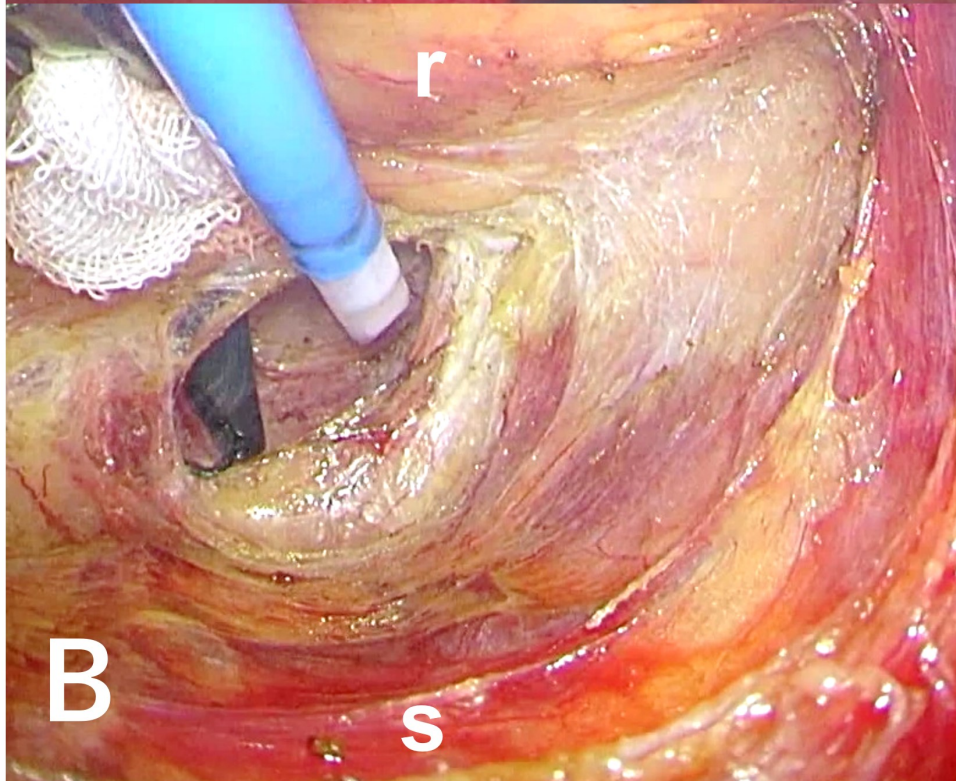
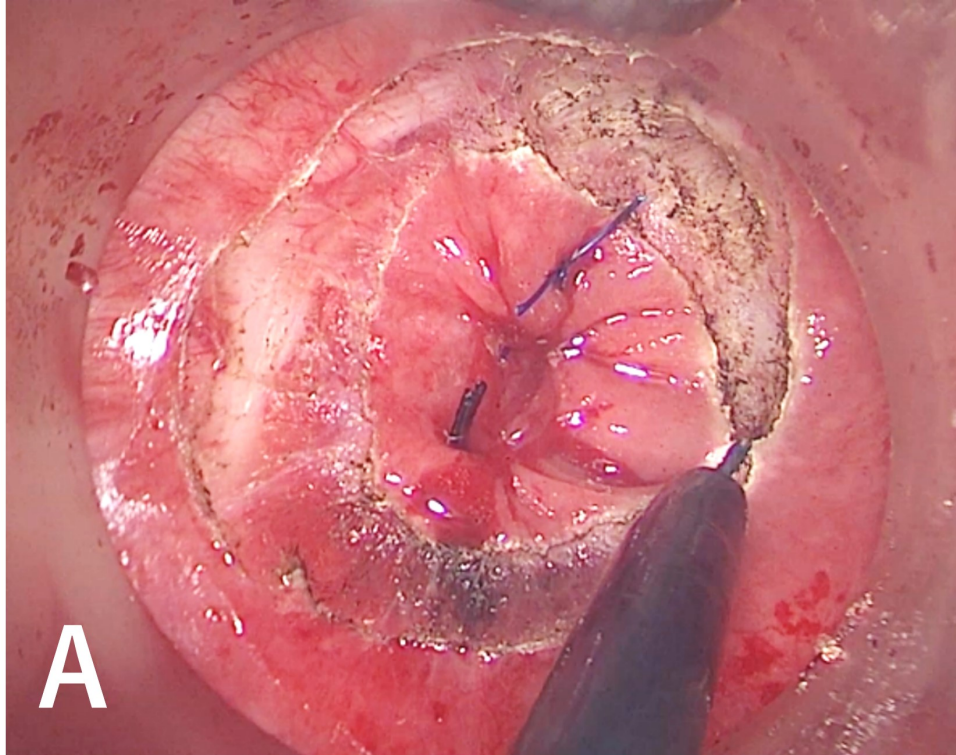


Table 1. Characteristics of previously reported patients with gynecological-related rectal-vaginal septal tumor in past 20 years.

Case	Reference, year	Age	Histological type	Immunohistopathology	Endometriosis	Treatment	Follow-up
1	Berger et al. [3], 2001	58	Adenocarcinoma	NA	-	AH+BSO+RR⇒RT	RE 5 years later
2	Papacharalabous et al. [13], 2004	57	Adenocarcinoma	NA	-	AH + BSO + RR	NED12months
3	Ulrich et al. [1], 2005	41	Adenocarcinoma	NA	+	RR+BSO+LN⇒RT	NED 2 years
4	Ulrich et al. [1], 2006	51	Adenocarcinoma	NA	+	BSO + LN + vagina, paracolpium resection + RR⇒RT	RE 2 years later
5	Yazbeck et al. [14], 2005	25	Adenocarcinoma	CK7(+), CK20(-)	+	CRT⇒AH+OM + LN + RR	NED 2 years
6	Guiou et al. [15], 2008	52	Clear cell adenocarcinoma	CK7(+)	-	CRT	NED
7	Langmár et al. [6], 2008	68	Adenocarcinoma	NA	-	TAH+BSO+RR⇒CT	N/A
8	Garg et al. [7], 2009	45	Endometrial stromal sarcoma	NA	+	PE⇒RT	N/A
9	Giordano et al. [8], 2010	37	Adenocarcinoma	CK7(+), CA125(+)	-	TAH+BSO+RR⇒CT	N/A
10	Mabrouk et al. [3], 2011	36	Mixed (clear cell and endometrioid) adenocarcinoma	CK7(+), ER (+)	+	LRH+BSO + LN+OM+RR⇒CT	NED 2 months
11	Fujimoto et al. [4], 2019	49	Adenocarcinoma	CK7(+), ER (+), CK20(-)	-	LH+BSO+RR+LN + vaginectomy ⇒ CT	DOD 14 months
12	Yang et al. [2], 2019	57	Endometrioid carcinoma	CK7(+), ER (+), PAX-8(+), CK20(-)	+	RH+BSO+LN+OM+AP+RR⇒CT	NED 6 months
13	Songmen et al. [16], 2020	35	Squamous cell carcinoma	NA	-	CRT	NED 4 months
14	Kim et al. [17], 2021	40	Endometrioid carcinoma	NA	+	L-RH+RR	NED 8 months
15	present case	48	Carcinosarcoma	CK7(+), ER (+), PAX-8(+), CK20(-)	-	NAC⇒TaTME⇒CT	NED 12months

AH; abdominal hysterectomy; BSO = bilateral salpingo-oophorectomy RR = rectal resection RT; irradiation therapy LN; lymphadenectomy CRT; chemoradiation therapy OM; omentectomy CT; chemotherapy PE; pelvic exenteration L-; laparoscopic RH; radical hysterectomy LH; laparoscopic hysterectomy AP; appendectomy NA = not available